

LETTERS TO THE EDITOR

Genes for intelligence on the X chromosome

The delightful letter by Turner and Partington¹ proposed that (1) genes associated with non-specific mental retardation determine human intelligence, (2) they are located primarily on the X chromosome, and (3) they were selected in polygynous males. A strict interpretation of their first point would require that all loci influencing intelligence have at least one allele causing non-specific mental retardation. They define non-specificity to mean "no somatic changes, no recognisable metabolic abnormalities, no other neurological signs, and no progression with age", which is therefore a failure to recognise an undiscovered abnormality. This point of their proposal cannot be confirmed nor disproven.

The number of autosomal recessive loci causing mental retardation has been estimated by two independent methods to be about 325, most, but not all, of them meeting the necessarily imprecise criteria for non-specificity.² The ratio of DNA in the X chromosome and autosomes is known from cytometry to be 0.054,³ and so by chance there should be about 17 loci on the X chromosome at which mutations for retardation may arise. With a Poisson distribution the standard error of this estimate is about $\sqrt{17}$, giving an upper limit of at least 25 X linked loci for retardation. Although new loci are still being discovered, it is not clear that the number of X linked loci (at present estimated at three) will exceed chance. The astonishingly high frequency of the fra(X) syndrome has no implication for the number of X linked loci that can cause retardation.

With respect to the third point, the model of a harem won by "exhaustive combat between adult males" has its charms. However, if these hypothetical conquests and rewards depended on what is now recognised as intelligence, sexual dimorphism for intelligence should be as great as for size. Since this is not the case in man or other mammals, raising children must have required as much intelligence as bashing other chaps or species.

Although Turner and Partington must be thanked for an attractive hypothesis, a special relation between the X chromosome and genes for intelligence, in the past or at present, is not supported.

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- 1 Turner G, Partington MW. Genes for intelligence on the X chromosome. *J Med Genet* 1991;28:429.
- 2 Morton NE. Effect of inbreeding on IQ and mental retardation. *Proc Natl Acad Sci USA* 1978;75:3906-8.
- 3 Morton NE. Parameters of the human genome. *Proc Natl Acad Sci USA* 1991;88:7474-6.

This letter was shown to Drs Turner and Partington who reply as follows.

We do not accept that "all loci influencing intelligence (should) have at least one allele

causing non-specific mental retardation". There are many mechanisms by which brain function can be compromised as a secondary effect, such as a metabolic error or aneuploidy. It is where the clinical picture is of mental retardation *only* that we suspect mutations in genes for intelligence.

Professor Morton has calculated that the number of recessive genes associated with mental retardation is 325; we do not argue with this but we do question whether such genes are for non-specific mental retardation. The data on which the calculations were made were derived mainly from studies in Japan where consanguinity is common and not class determined. The total study group was approximately 4000 school children. The authors state that the intellectually handicapped were integrated into these schools. There was no documentation of any attempt at diagnosis of the autosomal recessive (or other) conditions that one might expect in this population, so that we do not know that they met even the "imprecise criteria for non-specificity".

Morton estimates from the physical size of the X chromosome that there may be 25 loci for genes 'associated' with mental retardation. The number of such genes in the McKusick catalogue is already three times as many and increasing rapidly. Among these are three locations for non-specific mental retardation (MRX). So far no genes for non-specific mental retardation have been located on autosomes, so the X chromosome even now is more important than he has calculated it should be.

You can imagine in prehistoric times an earlier version of Morton's maternally derived X chromosomal DNA. Here he comes, out of the evening mist into the cave, pulling the beast he has trapped using an IQ now employed in writing letters to editors. Surely it would be the most intelligent, buxom wench in the flickering firelight who would say "Aargh!", decide "that's for me", and plan for the intertwining of two advantageous X chromosomes.

Morton's arguments are similar to those of Penrose when he failed to recognise the importance of genes on the X chromosome in the aetiology of mental retardation and are similar to those put forward against Lehrke's hypothesis. However, the clinical facts speak for themselves: one third of mental retardation is the result of genes on the X chromosomes and this cannot be refuted by theory.

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Another human homologue for the mouse mutant disorganisation

I read with interest the paper by Lowry and Yong¹ in which two brothers with cleft lip and palate, sensorineural deafness, and sacral lipoma were described. In addition, aberrant digits and an anterior sacral meningocele were found.

Recently I had the opportunity to investigate a male newborn with similar features. He was the first child born to non-consanguineous Caucasian parents. The father had had unilateral postaxial polydactyly, which was removed in the neonatal period. The family history was otherwise unremarkable. The mother denied any exposure to teratogenic agents during pregnancy. The boy was born prematurely (36 weeks), weighing 2500 g (25th centile). He had an occipital aplasia cutis, 2 cm in diameter. The underlying calvarium was absent, but there was no bulging encephalocele. Furthermore, he had a right sided cleft lip and bilateral cleft palate, hypoplasia of the abdominal musculature, slight flexion contracture of the right knee, and a right club foot. On the medial side of the left upper arm a 2 cm long, digit-like appendage without a nail was present.

The skull defect was closed on the first day of life and the appendage was removed. Histologically it consisted of normal cutis and subcutis without cartilage or bone. Further investigations, including radiography of the whole body, CT scanning of the brain, renal sonography, ophthalmological investigations, and karyotyping of lymphocytes showed no other anomalies. Auditory brainstem evoked potentials were normal. He had no somatic problems, especially no obstipation. Subsequent growth and development were normal.

This unusual combination of symptoms resembles those described in the sibs by Lowry and Yong,¹ and is similar to the manifestations in the mouse mutant disorganisation.² Another possible case of a human homologue of this mouse gene was recently described by Viljoen and Kidson,³ as pointed out by Winter and Donnai,⁴ and by Naguib *et al.*⁵ Several other cases can be found in older publications.⁶⁻⁹

The postaxial polydactyly in the father of the present boy may be coincidental, but may also be a clue to an autosomal dominant pattern of inheritance with variable expression. The presence of anomalies in two sibs without visible symptoms in the parents, as described by Lowry and Yong,¹ may be explained by germinal mosaicism or non-penetrance, as was reported in the mouse mutant.¹⁰

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- 1 Lowry RB, Yong SL. Cleft lip and palate, sensorineural deafness, and sacral lipoma in two brothers: a possible example of the disorganisation mutant. *J Med Genet* 1991;28:135-7.
- 2 Winter RM, Donnai D. A possible human homologue for the mouse mutant disorganisation. *J Med Genet* 1989;26:417-20.
- 3 Viljoen DL, Kidson SH. Mirror polydactyly: pathogenesis based on a morphogen gradient theory. *Am J Med Genet* 1990;35:229-35.
- 4 Winter RM, Donnai D. 'Disorganization' gene in mutations. *Am J Med Genet* 1990;37:435.
- 5 Naguib KK, Hamoud MS, Khalil ES, El-Khalifa MY. Human homologue for the mouse mutant disorganisation: does it exist? *J Med Genet* 1991;28:138-9.
- 6 Ollerenshaw R. Congenital defects of the long bones of the lower limb. *J Bone Joint Surg (Br)* 1925;7:528-52.
- 7 Ahlfeld F. *Die Missbildungen des Menschen*. Berlin, 1880.
- 8 Forster A. *Die Missbildungen des Menschen*. Jena, 1861.
- 9 Licetus F. *De monstros*. Padua, 1668.
- 10 Hummel PK. Developmental anomalies in mice resulting from action of the gene Disorganization, a semi-dominant lethal. *Pediatrics* 1959;23:212-21.